REMARKS

Claims 1-21 were examined. Claims 1, 3, 5, 7, 9-11, 13-15, 17, and 18-21 are amended. Claims 2, 6, 8, 12 and 16 are canceled. Claims 1, 3-5, 7, 9-11, 13-15 and 17-21 remain in the Application.

The Patent Office objects to the sequence listing. The Patent Office objects to claims 2, 5-6, 8, 11-14, 16, 19 and 21 for certain informalities. The Patent Office rejects claim 19 under 35 U.S.C. §112, second paragraph. The Patent Office rejects claims 1, 7, 15 and 20 under 35 U.S.C. §§102(e) and 102(b). The Patent Office rejects claims 2, 8 and 16 under 35 U.S.C. §103(a). Reconsideration of the pending claims is respectfully requested in view of the above amendments and the following remarks.

A. Sequence Rules

The Patent Office requests that the Application be amended to comply with the sequence rules. Applicants amend the Application as directed by the Patent Office to reference particular sequence ID numbers. Applicants also include herewith additional Sequence ID Nos. 12-15 corresponding to the primers listed at pages 14-15 of the Application. A substitute copy of the complete Sequence Listing, including Sequence ID Nos. 12-15 is submitted herewith as is a substitute computer readable form (CRF) copy of the Sequence Listing on 3.5 inch (1.44 Mb storage) diskette.

B. Claim Objections

The Patent Office objects to claims 2, 5-6, 8, 11-14, 16, 19 and 21 because of certain informalities. Applicants address herein the concerns raised by the Patent Office. Applicants respectfully request that the Patent Office withdraw the claim objections to noted claims.

C. 35 U.S.C. §112, Second Paragraph: Rejection of Claim 19

The Patent Office rejects claim 19 under 35 U.S.C. §112, second paragraph, as indefinite. Applicants amend claim 19. Applicants respectfully request that the Patent Office withdraw the rejection to claim 19 under 35 U.S.C. §112, second paragraph.

D. 35 U.S.C. §102(e): Rejection of Claims 1, 7, 15 & 20

The Patent Office rejects claims 1, 7, 15 and 20 under 35 U.S.C. §102(e) as anticipated by U.S. Patent No. 6,284,492 issued to Donson et al. (Donson).

Claim 1 describes a production system of the heterologous protein comprising a suitable promoter for producing a heterologous protein, a vector comprising an HCMV MIEP promoter, and an avian cell.

The HCMV MIEP promoter is the most powerful promoter for expressing heterologous protein in an avian cell. When levels of heterologous gene expression between different promoters such as the SV40 early promoter, the HCMV MIEP, and the RSV LTR and different host cells were compared, the heterologous gene was expressed very efficiently under the control of the HCMV MIEP promoter. In addition, when the vector comprising the HCMV MIEP promoter was used, the avian cells produced higher levels of heterologous protein than any other cell lines.

As described in the Application, the expression of the heterologous gene under the HCMV MIEP promoter was effective. See Application at page 12, line 9 to page 13, line 20, and page 17, line 2 to page 18, line 29. When the HCMV MIEP was used, the avian cell produced higher levels of heterologous protein than any other cell. See Application at page 12, line 9 to page 13 line 20, page 17, line 2 to page 18, line 29, and page 20 lines 14-29.

On the other hand, the expression method of protein using the avian cell as a host cell was known, but the method using the QT-VC cell was not. The QT-VC cell sub-cloned from QT6 grows faster than its parental line and it has a 12-24 hour doubling time, while the doubling time of QT6 is 24-36 hours, as shown in page 20 lines 1 and 11. Therefore QT-VC is a new cell line and it influences expression of the heterologous protein.

Donson describes a recombinant animal viral vector. The recombinant animal viral vector is self-replicating, capable of systemic infection of the host cell, and it contains foreign nucleic acids. For EPO production, a suitable promoter, a host cell, a method of expressing EPO, and data showing biological activity of recombinant EPO protein were not disclosed, and it is not expected that an EPO production system using the HCMV MIEP promoter and the avian cell is very effective or a more desirable system than that using other promoters and host cells.

Claim 7 recites a method of producing EPO including inserting an HCMV MIEP promoter into a vector, transfecting the vector into an avian cell, and culturing the avian cell. As noted above, Donson does not describe a method of producing EPO as claimed.

Claim 15 relates to an avian cell as a host for expressing EPO by controlling an HCMV MIEP promoter. As noted above, Donson does not describe such a cell.

Claim 20 relates to a method of producing human heterologous protein comprising inserting a DNA encoding a protein into a vector comprising an JCMV MIEP promoter; transfecting the vector into a cell; and culturing the transfected cell. Claim 21 describes the EPO protein as EPO. As noted above, Donson does not describe such a method.

Applicants respectfully request that the Patent Office withdraw the rejection to claims 1, 7, 15 and 20 under 35 U.S.C. §102(e).

E. 35 U.S.C. §102(e): Rejection of Claim 20

The Patent Office rejects claim 20 under 35 U.S.C. §102(e) as anticipated by U.S. Patent No. 5,968,823 issued to Bordon et al. (Bordon). Bordon was filed on May 31, 1996, after the priority date of August 24, 1995 of the Application. Submitted herewith is a copy of Korean Patent Application No. 1995-0026391 and a certified translation of the document.

Applicants respectfully request that the Patent Office withdraw the rejection to claim 20 as anticipated by Bordon.

F. 35 U.S.C. §102(b): Rejection of Claims 1, 7, 15 & 20-21

The Patent Office rejects claims 1, 7, 15 and 20-21 under 35 U.S.C. §102(b) as anticipated by U.S. Patent No. 5,162,215 issued to Bosselman et al. (Bosselman).

Bosselman relates to a method for introducing a replication-defective retroviral vector into pluripotent stem cells. The method is used for introducing foreign genetic material into somatic and germ cells resulting in the production of a transgenic chicken. In Bosselman, avian cells are used only for generating the transgenic chicken, and not for EPO production as described in the pending claims.

Applicants respectfully request that the Patent Office withdraw the rejection to claims 1, 7, 15 and 20-21 under 35 U.S.C. §102(b) in view of Bosselman.

G. 35 U.S.C. §103(a); Rejection of Claims 2, 8 & 16

The Patent Office rejects claims 2, 8 and 16 under 35 U.S.C. §103(a) as obvious over Bosselman in view of Bordon. In view of the above remarks with regard to Bosselman and the fact that Bordon is not prior art, Applicants respectfully request that the Patent Office withdraw the rejection to the claims under 35 U.S.C. §103(a).

CONCLUSION

In view of the foregoing, it is believed that all claims now pending patentably define the subject invention over the prior art of record and are in condition for allowance and such action is earnestly solicited at the earliest possible date.

Respectfully submitted,

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I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Assistant Commissioner for Patents, Washington, D.C. 20231 on February 4, 2002.

Nedy Calderon 2/4/02

Nedy Calderon Date

ATTACHMENT: VERSION WITH MARKINGS TO SHOW CHANGES MADE

VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE SPECIFICATION

The paragraphs on page 5, beginning at line 15 and ending on page 6, line 3, have been amended as follows:

Fig. 5 is various EPO genomic DNA sequences. ~~SY, SH, HE and JM~~ SY(SEQ ID NO:3), JM(SEQ ID NO:4), SH(SEQ ID NO:5), and HE(SEQ ID NO:6) are the EPO genomic DNA sequences cloned by the present invention, and ~~AM and GI~~ AM(SEQ ID NO:1) and GI(SEQ ID NO:2) are the EPO genomic sequences which has been already reported. Since the intron between the first coding region and the second coding region was deleted during the cloning, the deleted intron is not shown in Fig. 5.

Fig. 6 is various EPO amino acid sequences. ~~SY, SH, HE and JM~~ SY(SEQ ID NO:8), SH(SEQ ID NO:10), HE(SEQ ID NO:11), and JM(SEQ ID NO:9) are the EPO amino acid sequences cloned by the present invention, and AM(SEQ ID NO:7) and GI(SEQ ID NO:7) ~~AM and GI~~ are the EPO amino acid sequences which have been already reported. The abbreviation of the amino acids are as follows:

A: alanine	R: arginine	N: asparagine	D: aspartic acid
C: cystein	Q: glutamine	E: glutamic acid	H: histidine
I: isoleucine	L: leucine	K: lysine	M: methionine
F: phenylalanine	P: proline	S: serine	
T: threonine	W: tryptophan	Y: tyrosine	V: valine

On page 14, lines 25-26, please replace the sentences as follows:

Primer #25 (sense, ~~5' to 3'~~ SEQ ID NO:12): GAAGCTGATAAGCTGATAACC

Primer #33 (antisense, ~~5' to 3'~~ SEQ ID NO:13): TGTGACATCCTTAGATCTCA

On page 15, lines 10-13, please replace the sentences as follows:

Primer #12 (sense, ~~5' to 3'~~SEQ ID NO:14):

CAAGCTTCGGAGATGGGGTGCACGAATGTCCTGCCTGGCTGTGGC

Primer #9 (antisense, ~~5' to 3'~~SEQ ID NO:15):

CAAGCTTTCATCTGTCCCCTGTCCTGC

IN THE CLAIMS

Claims 2, 6, 8, 12 and 16 have been canceled.

The following claims have been amended:

1. (Amended) An EPO production system comprising:

a DNA encoding EPO;

a vector comprising an HCMV MIEP promoter for receiving the DNA; and

an avian cell for harboring the vector.

3. (Amended) The EPO production system of claim ~~2~~1, wherein the avian cell ~~QT~~ is QT-VC.

4. The EPO reproduction system of claim 1, wherein the DNA is a genomic DNA encoding EPO.

5. (Amended) The EPO production system of claim 1, wherein the DNA encoding EPO is SH (SEQ ID NO: 5)~~selected from the group consisting of SY, JM, SH and HE described in Fig. 5~~.

7. (Amended) A method of producing EPO comprising ~~the steps of~~:

inserting a DNA encoding an EPO into a vector comprising an HCMV MIEP promoter;

transfecting the vector into an avian cell; and

culturing the transfected avian cell in media.

9. (Amended) The method of claim ~~8~~7, wherein the ~~QT~~ avian cell is QT-VC.

10. The method of claim 7, wherein the DNA encoding EPO is a genomic DNA.

11. (Amended) The method of claim 7, wherein the DNA encoding the EPO is SH (SEQ ID NO: 5)~~selected from the group consisting of SY, JM, SH and HE described in Fig. 5~~.

13. (Amended) An EPO genomic sequence selected from the group consisting of SH (SEQ ID NO: 5)~~SY, JM, SH and HE described in Fig. 5~~.

14. (Amended) An EPO amino acid sequence selected from the group consisting of SH (SEQ ID NO: 10)~~JM, SH and HE described in Fig. 6~~.

15. (Amended) An avian cell as a host for expressing EPO by controlling an HCMV MIEP promoter ~~a gene encoding an EPO~~.

17. (Amended) The avian cell of claim ~~16~~15, wherein the ~~QT~~ avian cell is QT-VC.

18. (Twice Amended) ~~The EPO production system of claim 14, wherein the DNA encoding EPO is selected from the group consisting of SY, JM, SH and HE, respectively described by SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 5, and SEQ ID NO: 6.~~ A human heterologous protein production system comprising:

a DNA encoding a human heterologous protein;

a vector comprising an HCMV MIEP promoter for receiving the DNA; and

an avian cell for harboring the vector.

19. (Amended) The human heterologous protein production system of claim 18, wherein the human heterologous protein is ~~selected from the group consisting of TPA, Factor VIII and~~ EPO.

20. (Amended) A method of producing a human heterologous protein comprising ~~the steps of~~:

inserting a DNA encoding a human heterologous protein into a vector comprising an HCMV MIEP promoter;

transfecting the vector into an avian cell; and

culturing the transfected avian cell in media.

21. (Amended) The method of claim 20, wherein the human heterologous protein is ~~selected from the group consisting of TPA, Factor VIII and~~ EPO.